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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/553,509	10/18/2005	Mitsuharu Hirai	TOYA114.010APC	4683

20995	7590	06/04/2007
KNOBBE MARTENS OLSON & BEAR LLP		
2040 MAIN STREET		
FOURTEENTH FLOOR		
IRVINE, CA 92614		

EXAMINER	
WILDER, CYNTHIA B	

ART UNIT	PAPER NUMBER
1637	

NOTIFICATION DATE	DELIVERY MODE
06/04/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

jcartee@kmob.com
eOAPilot@kmob.com

Office Action Summary

Application No.

10/553,509

Applicant(s)

HIRAI, MITSU HARU

Examiner

Cynthia B. Wilder, Ph.D.

Art Unit

1637

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 21 March 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-9 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-9 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

FINAL ACTION

1. Applicant's amendment filed 3/21/2007 is acknowledged and has been entered. Claims 1-9 are pending and discussed in this Office action. All of the arguments have been thoroughly reviewed and considered but are not found persuasive for the reasons discussed below. Any rejection not reiterated in this action has been withdrawn as being obviated by the amendment of the claims.

This action is made FINAL.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Previous Rejections

3. The objection to the priority documents is withdrawn in view of Applicant's arguments. The prior art rejection under 35 USC 103(a) is maintained and discussed below.

4. **Issue I. Claims 1-2, and 7-9 are rejected under 35 USC 103(A) as being unpatentable over Shuldiner et al in view of Hiratsuka et al.**

Applicant's traversal

(I) Applicant traverses the rejection on the following grounds: Applicant states that the nucleic acid probes of the claimed invention have a nucleotide sequence starting at nucleotide 183 of SEQ ID NO: 1 and a length of 8 to 30 nucleotides or a nucleotide sequence ending at nucleotide 196 of SEQ ID NO: 2 and a length of 7 to 30 nucleotides. Applicant states that this feature is not taught by either of the cited

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references. Applicant states that neither Shuldiner nor Hiratsuka et al teach probes having the specific endpoint as claimed. Applicant states that among the many cytosines that could be labeled for detection of $\beta 3$ Adrenaline receptor mutations, the cytosines at 183 of SEQ ID NO: 2 and 196 of SEQ ID NO: 2 are critical for detecting the Trp64Arg mutation by Tm analysis. Applicant states that when probes as claimed are used, which have cytosine at the 5' end (position 183) or 3' (position 196), changes in fluorescence intensity that could be analyzed by Tm analysis were observed. Applicant states however, when probes having cytosine other than cytosine 183 or 196 at the 5' or 3' end, respectively, were used, changes in fluorescence intensity were not observed. Applicant states that Shuldiner, et al discloses only a part of the nucleotide sequence having the $\beta 3$ AR mutation and fails to teach the criticality of nucleotides 183 and 196. Applicant states that Shuldiner et al do not teach or suggest that the cytosine at position 183 and 196 corresponds to the 5' end and 3' end of the probes respectively. Applicant states that this deficiency is not corrected by Hiratsuka et al. Applicant states that Hiratsuka et al discloses a probe labeled with fluorescence tag and a method for detecting single nucleotide polymorphisms by using the probe. Applicant states that the claims do not teach the specific positions in the probes as claimed. Applicant states that accordingly, one of ordinary skill in the art would not have a reasonable expectation of success in achieving the claimed invention by combining Shuldiner et al and Hiratsuka et al. Applicant states that the importance of the cytosines at positions 183 and 196 for the 5' and 3' ends of the probe, respectively, could not have been predicted based upon the cited references. Applicant asserts that the claims 2-9 are

believed to patentable at least because they include all of the limitations of claim 1, which Applicant asserts is patentable for the reasons given above. Applicant request reconsideration and withdrawn of the rejections.

Examiner's Response

(ii) All of the arguments have been thoroughly reviewed and considered but are not found persuasive for the reasons that follow: In regards to Applicant arguments that the references does not teach the instant invention or the criticality of the cytosine at position 183 of SEQ ID NO: 1 and 196 of SEQ ID NO: 2, the Examiner respectfully disagrees. Firstly, the courts have established that during patent examination the pending claims must be interpreted as broadly as their terms reasonably allow (*In re Zletz*, 893 F.2d 321-22, 13 USPQ2d 1320, 1322 (Fed. Cir. 1989). In this case, the claims as broadly written do not require that a cytosine or any other specific base be position at nucleotide 183 of SEQ ID NO: 1. The claims only require that the probe sequence start at position 183 of SEQ ID NO: 1 and have a length of 8 to 30 nucleotides and the 5' end labeled with a fluorescent dye. Alternatively, the claims require that the nucleotide probe end at the nucleotide number 196 in the nucleotide sequence of SEQ ID NO: 2 and having a length of 7 to 30 nucleotides and wherein the 3' end of the probe is labeled with a fluorescent dye. The claims, especially claim 2, suggest that the probe comprising the sequences as recited in SEQ ID NOS: 8-12 corresponds to the probe as broadly recited in the claim 1.

Thus, contrary to Applicant's arguments, the prior art of Shuldiner does teach the instant invention as claimed. Shuldiner et al provides a probe nucleotide sequence that is 100% identical to the sequences of SEQ ID NOS: 11 and 12 (SEE SEQ ID NO: 7 and Appendix A, B and C at this end of this Office action). An alignment of this sequence with the sequence of SEQ ID NO: 1 shows that this sequence begins at nucleotide 183 of SEQ ID NO: 1. Additionally, while the claim does not require that a cytosine be present at position 183, the sequence of Shuldiner provides this teaching as well as a cytosine is present at the first position or 5' end of the probe of Shuldiner et al (see SEQ ID NO: 7 at col. 25 or Appendix A). Further, Shuldiner teaches wherein the probe meets the length limitation of the probe of claim 1 (Shuldiner teach wherein the probes are 17 nucleotides in length) and additionally teaches wherein the probe is used to detect the Trp64Arg mutation (see columns 11, 12, 17 and 18). The secondary reference of Hiratsuka provides the limitations not found in the patent of Shuldiner and provides motivation for combining the teachings. Applicant's arguments are not sufficient to overcome the prior art rejections. Accordingly, the rejections are maintained.

5. **Issue II. Claims 3-6 are rejected under 35 USC 103(A) as being unpatentable over Hiratsuka et al in view of Shuldiner et al as previously applied above.**

Applicant's traversal and Examiner's Response

(I) Applicant traverses the rejection on the same grounds presented above at number 4. The Examiner in response asserts that Applicant's arguments are not

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sufficient to overcome the prior art rejections under 35 USC 103(a) and in conclusion maintains the rejections for the reasons discussed above.

Conclusion

6. No claims are allowed. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

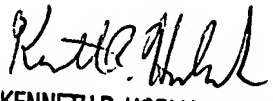
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cynthia B. Wilder, Ph.D. whose telephone number is (571) 272-0791. The examiner can normally be reached on a flexible schedule.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Cynthia B. Wilder, Ph.D.
Patent Examiner
Art Unit 1637


KENNETH R. HORLICK, PH.D.
PRIMARY EXAMINER
5/24/07

Appendix A

5,766,851

25

26

-continued

(i i) MOLECULE TYPE: DNA (genomic)

(x i) SEQUENCE DESCRIPTION: SEQ ID NO:7:

CATCGCCTGG ACTCCGA

(2) INFORMATION FOR SEQ ID NO:8:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 17 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

(i i) MOLECULE TYPE: DNA (genomic)

(x i) SEQUENCE DESCRIPTION: SEQ ID NO:8:

CATCGCCCGG ACTCCGA

(2) INFORMATION FOR SEQ ID NO:9:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 22 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

(i i) MOLECULE TYPE: DNA (genomic)

(x i) SEQUENCE DESCRIPTION: SEQ ID NO:9:

GAAAGGGGAC AGATCTCACC AA

(2) INFORMATION FOR SEQ ID NO:10:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 19 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

(i i) MOLECULE TYPE: DNA (genomic)

(x i) SEQUENCE DESCRIPTION: SEQ ID NO:10:

TTCCTCTGCC ACCATCTGT

(2) INFORMATION FOR SEQ ID NO:11:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 20 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

(i i) MOLECULE TYPE: DNA (genomic)

(x i) SEQUENCE DESCRIPTION: SEQ ID NO:11:

CCAGGGAGTG CTATGCTGAG

(2) INFORMATION FOR SEQ ID NO:12:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 24 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

(i i) MOLECULE TYPE: DNA (genomic)

(x i) SEQUENCE DESCRIPTION: SEQ ID NO:12:

100% Identical to SEQ ID NO: 11 + 12 of the
Instant invention.

Appendix B

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<!--StartFragment-->US-08-446-530-7
; Sequence 7, Application US/08446530
;.Patent No. 5766851
; GENERAL INFORMATION:
; APPLICANT: Shuldiner, Alan R.
; APPLICANT: Walston, Jeremy
; APPLICANT: Silver, Kristi
; TITLE OF INVENTION: SUSCEPTIBILITY GENE FOR OBESITY AND TYPE
; TITLE OF INVENTION: II DIABETES MELLITUS
; NUMBER OF SEQUENCES: 28
; CORRESPONDENCE ADDRESS:
; ADDRESSEE: Fish & Richardson P.C.
; STREET: 4225 Executive Square
; CITY: La Jolla
; STATE: CA
; COUNTRY: USA
; ZIP: 92037
; COMPUTER READABLE FORM:
; MEDIUM TYPE: Floppy disk
; COMPUTER: IBM PC compatible
; OPERATING SYSTEM: PC-DOS/MS-DOS
; SOFTWARE: PatentIn Release #1.0, Version #1.30
; CURRENT APPLICATION DATA:
; APPLICATION NUMBER: US/08/446,530
; FILING DATE: 19-MAY-1995
; CLASSIFICATION: 435
; ATTORNEY/AGENT INFORMATION:
; NAME: Haile, Lisa A.
; REGISTRATION NUMBER: 38,347
; REFERENCE/DOCKET NUMBER: 07265/048001
; TELECOMMUNICATION INFORMATION:
; TELEPHONE: 619/678-5070
; TELEFAX: 619/678-5070
; INFORMATION FOR SEQ ID NO: 7:
; SEQUENCE CHARACTERISTICS:
; LENGTH: 17 base pairs
; TYPE: nucleic acid
; STRANDEDNESS: single
; TOPOLOGY: linear
; MOLECULE TYPE: DNA (genomic)
US-08-446-530-7

```

→ to SEQ ID NO: 11

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Query Match          100.0%; Score 16; DB 2; Length 17;
Best Local Similarity 100.0%; Pred. No. 30;
Matches 16; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

```

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Qy      1 CATCGCCTGGACTCCG 16
        |||||
Db      1 CATCGCCTGGACTCCG 16

```

<!--EndFragment-->

<!--StartFragment-->RESULT 2
US-08-446-530-7
; Sequence 7, Application US/08446530
; Patent No. 5766851

Appendix C

; GENERAL INFORMATION:
; APPLICANT: Shuldiner, Alan R.
; APPLICANT: Walston, Jeremy
; APPLICANT: Silver, Kristi
; TITLE OF INVENTION: SUSCEPTIBILITY GENE FOR OBESITY AND TYPE
; TITLE OF INVENTION: II DIABETES MELLITUS
; NUMBER OF SEQUENCES: 28
; CORRESPONDENCE ADDRESS:
; ADDRESSEE: Fish & Richardson P.C.
; STREET: 4225 Executive Square
; CITY: La Jolla
; STATE: CA
; COUNTRY: USA
; ZIP: 92037
; COMPUTER READABLE FORM:
; MEDIUM TYPE: Floppy disk
; COMPUTER: IBM PC compatible
; OPERATING SYSTEM: PC-DOS/MS-DOS
; SOFTWARE: PatentIn Release #1.0, Version #1.30
; CURRENT APPLICATION DATA:
; APPLICATION NUMBER: US/08/446,530
; FILING DATE: 19-MAY-1995
; CLASSIFICATION: 435
; ATTORNEY/AGENT INFORMATION:
; NAME: Haile, Lisa A.
; REGISTRATION NUMBER: 38,347
; REFERENCE/DOCKET NUMBER: 07265/048001
; TELECOMMUNICATION INFORMATION:
; TELEPHONE: 619/678-5070
; TELEFAX: 619/678-5070
; INFORMATION FOR SEQ ID NO: 7:
; SEQUENCE CHARACTERISTICS:
; LENGTH: 17 base pairs
; TYPE: nucleic acid
; STRANDEDNESS: single
; TOPOLOGY: linear
; MOLECULE TYPE: DNA (genomic)

US-08-446-530-7

→ to SEQ ID NO. 12

Query Match 100.0%; Score 15; DB 2; Length 17;
Best Local Similarity 100.0%; Pred. No. 54;
Matches 15; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 CATCGCCTGGACTCC 15
| | | | | | | | | | | | | | | | |
Db 1 CATCGCCTGGACTCC 15
<!--EndFragment-->